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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,591	08/16/2006	Pann-Ghill Suh	20010-21USA	3560

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EXAMINER
MOHAMED, ABDEL A

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
02/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,591	SUH ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *7-11 and 15-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,12-14 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/31/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT TO PRIORITY, IDS, AMENDMENT, RESPONSE TO RESTRICTION REQUIREMENT, STATUS OF THE APPLICATION AND CLAIMS

1. This application is filed under 35 U.S.C. 371 on 08/16/06 having a filing date of 02/03/05 of PCT/KR2005/000329, which claims benefits of U.S. Provisional application No. 60/541,730 having a filing date of 02/04/04. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file. The information disclosure statement (IDS) and Form PTO-1449 filed 07/31/06, amendment and the response to the restriction requirement filed 11/26/08, respectively are acknowledged, entered and considered. In view of Applicant's request claims 6 and 14 have been amended. Claims 1-20 are now pending in the application.

ELECTION WITH TRAVERSE

2. Applicant's election with traverse of Group I and SEQ ID NO:4 (claims 1-13 and 20) in the communication filed 11/26/08 is acknowledged. The traversal is on the ground(s) that the restrictions of the claims into six groups are improper because all the claims revolve around inventive W-rich peptides and their use. Therefore, all of the claims are unified and belongs to a single inventive concept. At the least, claim 14 belonging to Group II should be joined to the Group I claims, since "arthritis" recited in claim 14 is caused by "inflammation" in claim 13 and claim 14 has been amended to depend from claim 13.

Further, Applicant contends that all of the claimed subject matter is related through the disclosure of the inventive peptides. The claims are directed to conservative variants and functional fragments thereof. All of the claimed peptides belong to a family of W-rich peptides, and have common activities such as prevention of inflammation, treatment of an auto-immune disease, prevention of binding of Aβ42 to human neutrophils, treatment of Alzheimer's disease, and interaction with FPR as recited in the claims. Therefore, the sequences are so close in structure that they should be examined together. In particular, at least the peptides with conservative substitutions and fragments should be examined together, as there would be little burden on the Examiner to search and consider these sequences. It would cause undue hardship on the Applicant to be forced to separate applications for each of these peptides, when clearly these peptides merely contain conservative amino acid substitutions is unpersuasive.

Contrary to Applicant's contention as stated in the previous Office action the methods of Groups I-VI do not correspond to the same technical features and are not connected in design, operation or effect because they differ in method steps, parameters and reagents used, although, the five groups use the same compounds as recited above, and as such, the method of Group I is directed to a method of preventing inflammation in a subject comprising the steps of providing an inflammation preventing effective amount of the polypeptide according to claim 1 or a W-rich peptide mimic thereof to the subject in need thereof. Group II is directed to a method of treating arthritis in a subject comprising the steps of providing an inflammation preventing

effective amount of the polypeptide according to claim 1 or a W-rich peptide mimic thereof to the subject in need thereof. Group III is directed to a method of treating an auto-immune disease in a subject comprising the steps of providing a therapeutically effective amount of the polypeptide according to claim 1 or a W-rich peptide mimic thereof to the subject in need thereof. Group IV is directed to a method of preventing binding of Aβ42 to human neutrophils comprising contacting the neutrophil with the polypeptide according to claim 1 or a W-rich peptide mimic thereof. Group IV is directed to a method of treating Alzheimer's disease comprising administering a therapeutically effective amount of the polypeptide according to claim 1 or a W-rich peptide mimic thereof to the subject in need thereof.

With respect to Group VI, this group differs from Groups I-V in using different compounds for different purposes. Group VI is directed to an assay method of identifying a FPR class receptor antagonist while Groups I-V are directed to various methods of treatment and prevention of different diseases and/or conditions using basically the same compounds for different purposes. Thus, Groups I-V are methods of treatment or prevention while Group VI is an assay method. Therefore, the methods of Groups I-VI as recited above do not correspond to the same technical features and are not connected in design, operations or effects because they differ in method steps, parameters and reagents used and functions, and as such, the methods as grouped are independent and distinct, each from the other because they represent different technical features and different inventive endeavors. Thus, the Groups require different patent and literature search and as such Groups I-VI do not share the same technical features,

the inventions do not relate to the same inventive concept. However, due to the amendment of claim 14 to "wherein the inflammation is arthritis", as amended claim 14 depend on claim 13, and as such, amended claim 14 belongs to Group I. Thus, claim 14 has been rejoined with Group I. Therefore, Group I is directed to claims 1-14 and 20.

In regard to Applicant's contention that it is proper to examine all SEQ ID NOS recited in claims 6-11 as one group for further prosecution is noted. However, Applicant's contention is not found persuasive for the reasons of record because the various sequences disclosed in claims 6-11 encompass peptides having different structures which are patentably distinct and/or independent, one from the other, and capable of independent use. Further, there is no sequence linking each with other, it is only consensus.

Therefore, the sequences are patentably distinct because they are unrelated sequences and each unrelated sequence is considered a separate and distinct product. For an elected invention drawn to either amino acid or polypeptide sequences, the Applicant must elect a **single** peptide sequence (See MPEP 803.04). Due to the increasing large size of sequence databases which must be searched and the increasing numbers of applications requiring sequence searches, it creates an undue burden on the Office to search more than a single sequence (product) per application. For these reasons, the requirement of 37 CFR 1.141 *et seq.* is no longer waived and Applicant is required to elect a **single** sequence for examination. Applicant is reminded that this is a **restriction requirement**, not an election of species as contended by

Applicant. Thus, they are unrelated and are different inventions having independent and distinct formulations, which are not connected in design, operation or effect.

It is noted that claims 6 to 11 comprise the elected SEQ ID NO:4 along with non-elected sequences (i.e., SEQ ID NOS:5-8 and 12-35). The elected SEQ ID NO:4 is disclosed in claims 6-11 and claims 7-11 depend directly on indirectly on claim 6. Thus, only claim 6 which is the first occurrence of SEQ ID NO:4 is examined along claims 1-5 12-14 and 20 as the elected Group I and SEQ ID NO:4. Therefore, sequences recited in claim 6 other than SEQ ID NO:4, claims 7-11 and 15-19 are withdrawn as non-elected invention and sequences for the reasons of record. Hence, the Office action is directed to the merits of claims 1-6 (only SEQ ID NO:4 in claim 6), 12-14 and 20 with SEQ ID NO:4 as *per* elected invention and sequence and Applicant is advised to cancel non-elected inventions of claims 7-11 which comprise non-elected SEQ ID NOS:5-8 and 12-35 as well as the methods of claims 15-19 (i.e., Groups III-VI) in the next communication.

The requirement is still deemed proper and is therefore made FINAL.

OBJECTION TO THE SPECIFICATION

3. The specification is objected in failing to recite the continuing data for PCT/KR2005/000329. Recitation of the priority in the first page of the specification would obviate this objection.

The disclosure is also objected to because of the following informalities: The description under Brief Description of the Drawings for Figure 8 (page 8) references

color (photograph obtained by confocal) stained with anti-Aβ42 antibody. However, the drawing is in black and white and thus the description is not consistent with the actual drawing. It may be necessary to file a petition and fee for color drawings and amend the specification and drawings appropriately. Appropriate correction is required.

OBJECTION TO TRADEMARKS AND THEIR USE

4. The use of the trademarks "TWEEN®" and "PLURONIC®" have been noted in this application. Although, the use of trademarks are permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in a manner, which might adversely affect their validity as trademarks.

Further, the specification, which specifies the generic terminology should include, published product information sufficient to show that the generic terminology or the generic description are inherent in the article referred by the trademarks. These description requirements are made because the nature and composition of article denoted by trademarks can change and affect the adequacy of the disclosure.

CLAIMS REJECTION-35 U.S.C. 112 1st PARAGRAPH.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are no teachings in the specification to show the enablement for a method of **preventing** inflammation in a subject by providing and/or administering therapeutically effective amount of the polypeptide according to claim 1 (i.e., W-rich peptide and a conservative variant or functional fragment thereof) or a W-rich peptide mimic thereof to a subject in need thereof, wherein the inflammation is arthritis as claimed in claims 13 and 14 because there are no working example(s) or data or evidence in the instant invention, except for protocols of evaluating and/or screening of W-rich peptides for their ability to bind to an formyl peptide receptor (FPR) as disclosed in Figures 1, 2, and 6-8 while Figures 3-5 show FPRL1 expressing RBL-2H3 cells. Further, Example 1 discloses materials and methods for FPRL1 antagonist peptide characterization, Example 2 demonstrates results of FPRL1 antagonist peptide characterization and Example 3 shows additional FPRL1 antagonist characterization. Although, there is disclosure for a pharmaceutical composition with a pharmaceutical acceptable carrier as disclosed in the protocols on pages 17-23 in the instant specification; however, there is no disclosure for a method of **preventing** inflammation in a subject , wherein the inflammation is arthritis by providing and/or administering therapeutically effective amount of the polypeptide according to claim 1 or a W-rich

peptide mimic of claim 12 to the subject in need thereof in the manner claimed in claims 13 and 14.

Thus, there is no evidence in the instant specification to provide or administer the pharmaceutical composition useful for a method of **preventing** inflammation wherein the inflammation is arthritis in a subject as claimed, except for the mere recitation of protocols on page 17, lines14 to page 18, lines 21 in the instant specification disclosing the treatment and/or prevention of auto-immune disease, neurodegenerative disease such as Alzheimer's disease, and prevention and/or reduction of inflammation as well as prevention and/or treatment of diseases associated with inflammations such as rheumatoid arthritis and osteoarthritis in subjects without presenting any data or evidence to substantiate the protocols. Hence, the only support for the claimed method of treatment or **prevention** using the pharmaceutical composition in the specification is Applicant's supposition of the invention as recited in the protocols.

Further, the burden of enabling the **prevention** of a disease (i.e., the need for additional testing) would be greater than that of enabling a treatment due to the need to screen those animals susceptible to such diseases and the difficulty of proof that the administration of the drug was the agent that acted to prevent the condition. Further, the instant specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to all kinds of inflammations in general and in particular to arthritis (i.e., an auto-immune disease) in a subject which encompasses human is within the scope of the presently claimed invention. Nor is guidance provided as a specific protocol to be utilized in order to prove the efficacy of

the presently claimed W-rich peptide or a W-rich peptide mimic in preventing inflammation in a subject including arthritis. Additionally, the specification even fails to enable "treatment" to the extent such treatment includes the prevention of a disease state. Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention's method of **preventing** inflammation in subjects wherein the inflammation is arthritis as claimed in claims 13 and 14.

Furthermore, as defined on page 10, lines 20 to 23 in the instant specification, "W-rich peptide" refers to an oligopeptide that may be from about 4 to about 15 amino acids long, wherein at least 50% of the amino acid content is tryptophan (both L- and D-forms). Further, the W-rich peptide is an antagonist to the FPR class receptor, and more particularly, the FPRL1 receptor. Also, on page 15, lines 15 to 25 in the instant specification, "W-rich peptide mimic" is defined as peptidomimetics, peptides, modified peptides, and derivatized peptides and thus, are members of the class of antagonist compounds. Additional antagonist compound derivatives include peptidomimetics that resemble a polypeptide of interest. The naturally occurring amino acid employed in the biological production of peptides all have the L-configuration. Synthetic peptides can be prepared employing conventional synthetic methods, utilizing L-amino acids, D-amino acids, or various combinations of amino acids of the two different configurations. Synthetic compounds that mimic the conformation and desirable features of a particular peptide, e.g., an oligopeptide, once such peptide has been found, but that avoids the

undesirable features, e.g., flexibility (loss of conformation) and bond breakdown are known as “peptidomimetics”.

Therefore, Applicants claims are directed to a very large number of compounds by using specific therapeutic effective amount of a pharmaceutical composition, and there is no objective factual evidence in the specification showing that treatment/prevention has occurred using the specific therapeutic effective amount of W-rich peptide or W-rich peptide mimic as claimed. Thus, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the use of various W-rich peptides or W-rich peptide mimics for the claimed purposes of preventing inflammation wherein the inflammation is arthritis. Hence, it would include those that have not been shown or taught to be useful or enabled by the disclosed methods of making and using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since the various W-rich peptide or W-rich peptide mimics are contemplated and are encompassed as well as wide range of situations. The results desired appear to be highly dependent on all variables, the relationships of which is not clearly disclosed. Thus, one cannot employ or use or provide and/or administer specific pharmaceutical composition in all situations without appropriate testing.

Therefore, without guidance through working example(s), one of ordinary skill in the art would not predict from the protocols disclosed incorporating various references to show the method for preventing inflammation to a subject by providing and/or administering polypeptide according to claim 1 or W-rich peptide mimic thereof

according to claim 12 to the subject in need thereof wherein the inflammation is arthritis in the manner claimed in claims13 and 14 in the instant invention. Thus, the specification does not enable any person skilled in the art to which it pertains, or which is most nearly connected, to use the invention commensurate in scope with the claim. In the express absence of one or more examples, evidence and sufficient guidance, the skilled artisan would be faced with undue experimentation for practicing the invention.

CLAIM REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite in failing to identify a W-rich peptide mimic because there is no functional or structural limitations recited in the claim. Further, it is not clear to what kind of W-rich peptide mimics are intended and to which kind? Clarity is lacking at the point of novelty since the novelty appears to be W-rich peptidomemtics thereof. Thus, Applicant has to point out and distinctly claim the subject matter which is novel.

CLAIM REJECTION-35 U.S.C. § 102(a)

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-6, 12 and 20 are rejected under 35 U.S.C. 102(a) as being anticipated by Bae et al (The Journal of Immunology, January 01, 2004, Vol. 173, No. 1, pages 607-614).

The instantly claimed invention of claims 1-6, 12 and 20 are directed to a polypeptide comprising a W-rich-peptide and a conservative variant or functional fragment thereof (claim 1), wherein the polypeptide are from 4-15 amino acids long (claim 2), 4-10 amino acids long (claim 3), 4-7 amino acids long (claim 4), 6 amino acids long (claim 5) or as represented by SEQ ID NO:4 i.e., WRWWWW (WRW^4) (claim 6), W-rich peptide mimic (claim 12) and a pharmaceutical composition comprising the polypeptide of claim 1 or W-rich peptide mimic thereof (claim 20).

The prior art of Bae et al discloses screening of a tryptophan-rich peptide (W-rich peptide) libraries to identify several hexapeptides including SEQ ID NO:4 (WRW^4) that antagonize formyl peptide receptor-like 1 (FPRL1) signaling, wherein the W-rich peptide, such as WRW^4 (SEQ ID NO:4) would be used to antagonistically block of Aβ42 peptide, wherein in terms of Alzheimer's disease, Aβ42 peptide is known to play a central role in mediating neurotoxicity and in the formation of senile plaque. The WRW^4 (SEQ ID NO:4) hexapeptide overlaps with the claimed ranges of 4-15, 4-10, 4-7 and 6 amino acid long of claim 2, 3, 4, 5, respectively (See abstract, results and discussion). On page 612, under discussion, the reference states that in the study by screening peptide libraries we identified several hexapeptides that are W-rich peptides which

includes W-rich peptide mimic. With regard to pharmaceutical composition, to the extent that the W-rich peptide or W-rich peptide mimic is in a physiological buffer it is considered to be a pharmaceutical composition. Thus, in the absence of evidence to the contrary, the claimed W-rich peptide including SEQ ID NO:4 comprising WRW^4, or 4-15, or 4-10, or 4-7 or 6 amino acids long or a W-rich peptide mimic and a pharmaceutical composition thereof disclosed by the prior art anticipates claims 1-6, 12 and 20 as drafted.

CITATION OF RELEVANT PRIOR ART

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Selsted et al (U.S. Patent No. 5,324,716) disclose the use of antimicrobial compound that includes a W-rich peptide exhibiting antimicrobial activity, but does not disclose the elected WRW_4 peptide.

WO 2005/024057 of Merchiers et al teaches a method of identifying a compound that changes the amyloid precursor protein processing in a cell using W-rich peptides.

Similarly, WO 2005/024058 of Merchiers et al discloses compounds useful for treating conditions such as Alzheimer's disease that act by reducing the level of amyloid-beta protein by using W-rich peptides such as WRW^4 (the elected SEQ ID NO:4). Although the priority document of Merchiers et al. would otherwise qualify Merchiers et al. as prior art, the priority document does not provide support for the elected WRW^4 peptide.

CONCLUSION AND FUTURE CORRESPONDANCE

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mohamed/A. A. M./
Examiner, Art Unit 1654

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657